Original Article

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Ophthalmology Section

Prevalence of Diabetic Retinopathy in Patients with Cerebrovascular Accident: A Cross-sectional Study

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ABSTRACT

Introduction: Diabetes Mellitus (DM) causes high blood sugar, leading to complications such as cerebrovascular events, chronic kidney disease, cardiovascular issues and retinopathy. Diabetic Retinopathy (DR) is a key microvascular complication and may indicate other diabetic issues. Studies suggest a link between DR and Cerebrovascular Accidents (CVAs) (strokes), particularly in low and middle-income countries where stroke rates are increasing.

Aim: To assess the prevalence of DR among individuals who have experienced CVAs and to explore the relationship between DR and CVAs within the Indian population.

Materials and Methods: The present cross-sectional study was conducted in the Department of Ophthalmology, Dr. D. Y. Patil Medical College and Research Centre (tertiary care hospital), Pimpri, Pune, Western Maharashtra, India, from November 2022 to June 2024. The study included 100 patients (200 eyes) aged 40-70 years with CVAs and diabetes. Details regarding age, gender and, detailed ocular and systemic information were recorded. Diagnosis of DM and CVA is done according to standard methods. Intraocular pressure was measured using the Goldmann Applanation Tonometer (GAT) and Optical Coherence Tomography (OCT). DR was classified based on severity into mild, moderate and severe groups. Data were analysed using Statistical Package for Social Sciences (SPSS) software version 26.0. Statistical significance was set at 5%.

Results: In the present study, patients with DR had a mean±Standard Deviation (SD) age of 57.13±7.63 years. Among the CVA patients, 79% had DR. A total of 44 (44%) patients had moderate Non Proliferative Diabetic Retinopathy (NPDR), 20 (20%) had mild NPDR and 15 (15%) had severe NPDR. The average age of DR patients was 57.13±7.63 years, compared to 51.48±6.36 years for non DR patients. Haemorrhagic strokes were more common, occurring in 59 (59%) patients. Patients with both DR and CVAs were older and had higher blood sugar and HbA1c levels than those without DR. No association was found between DR and the type of stroke (p-value 0.761).

Conclusion: Diabetic retinopathy was present in 79% of stroke patients, with moderate NPDR being the most common type. DR patients were older and had higher blood sugar and HbA1c levels. Haemorrhagic stroke was more prevalent in this group. However, no significant association was found between the types of stroke and DR.

Keywords: Glycated haemoglobin, Haemorrhagic stroke, Ischaemic stroke, Random blood sugar level

INTRODUCTION

Diabetes mellitus encompasses a range of metabolic disorders characterised by persistent high blood sugar levels (hyperglycaemia). Common symptoms include frequent urination, increased thirst and heightened hunger. Poorly managed DM can lead to severe complications such as diabetic ketoacidosis, hyperosmolar hyperglycaemic state, or even death. Long-term consequences include CVAs, chronic kidney disease, cardiovascular conditions, foot ulcers, neuropathy, retinopathy and cognitive decline. DM develops from either inadequate insulin production by the pancreas or an ineffective response of cells to insulin. Insulin, a hormone, facilitates the uptake of glucose from the bloodstream into cells for energy production [1].

Diabetic retinopathy, a chronic microvascular complication of DM, may manifest as an initial sign of further diabetic issues. Approximately 35% of people with DM develop DR, with 20% progressing to proliferative DR [2]. Among working-age individuals, DR stands as the leading cause of moderate-to-severe vision loss [3]. Vision impairment due to DR not only diminishes a patient's quality of life but also complicates disease management, potentially leading to diabetes-related mortality.

Diabetes mellitus is a complex illness with a broad spectrum of clinical presentations. Factors such as the duration of diabetes, glycated Haemoglobin (HbA1C) levels, systolic blood pressure and total cholesterol are well-established risk factors associated with the development of DR [2,4]. CVAs (strokes) represent a significant cause of mortality and long-term disability globally, constituting an epidemic. While stroke incidence has declined by 42% in high-income countries from 1990 to 2016, it has doubled in low and middle-income countries. The Global Burden of Disease Study (GBD) highlights that although the frequency of strokes has decreased, their socio-economic impact has escalated due to factors such as demographics and geographic distribution [5].

There is a notable lack of studies from India addressing the relationship between DR and stroke among diabetes patients. Therefore, the present study aimed to explore the association between CVAs and DR, investigating whether early retinopathy screening should be mandated as part of a comprehensive protocol for managing patients with CVAs. The present study seeks to assess the prevalence of DR among individuals who have experienced CVAs and to explore the relationship between DR and CVAs within the Indian population.

MATERIALS AND METHODS

The present cross-sectional study was conducted in the Department of Ophthalmology, Dr. D. Y. Patil Medical College and Research Centre (tertiary care hospital), Pimpri, Pune, Western Maharashtra, India, from November 2022 to June 2024. The study was approved by the Institutional Ethics Committee of the study Institute (IESC/PGS/2022/369).

Inclusion criteria: All patients diagnosed with CVAs and DM, aged 40-70 years, at a tertiary care hospital in Western Maharashtra were included in the study.

Exclusion criteria: Patients with mature cataracts, pre-existing corneal opacities due to degeneration or dystrophies, any other ocular co-morbidities such as glaucoma, a history of vitreoretinal surgeries, or those unwilling to participate were excluded from the study.

Sample size calculation: The minimum sample size was determined to be 100 using WinPepi software [6]. Prior to inclusion, all patients provided written consent, ensuring ethical integrity and respecting participant autonomy throughout the study.

Study Procedure

The present study included 200 eyes from 100 patients diagnosed with both CVAs and DM, aged 40-70 years. A comprehensive history was collected, encompassing age, gender and detailed ocular and systemic information. This included documenting current ocular symptoms, if present, as, well as pertinent past histories such as ocular diseases, trauma, or surgeries. Additionally, details regarding the diagnosis and duration of CVAs and DM were recorded. A diagnosis of DM was made based on criteria such as a random plasma glucose level of 200 mg/dL or higher, along with classic symptoms including polydipsia, polyuria, unexplained weight loss and an HbA1C level greater than 6.5% [7]. CVA was diagnosed based on a detailed history, symptoms such as slurring of speech, paresis, paralysis, deviation of the mouth, cognitive decline and confirmation through radioimaging, either CT or Magnetic Resonance Imaging (MRI) [8]. Intraocular pressure was measured using the GAT and OCT was performed for posterior segment evaluation wherever indicated. DR was classified based on severity into mild, moderate and severe groups [9].

STATISTICAL ANALYSIS

Data were recorded in Microsoft Excel and analysed using SPSS software version 26.0. Quantitative data were presented as mean±SD and median Interquartile Range (IQR), while qualitative data were summarised using proportions. Due to the skewed distributions of continuous variables, the Mann-Whitney U test and Kruskal-Wallis test were used to assess differences between continuous and categorical variables, respectively. The Chi-square test was employed to examine associations among categorical variables. Statistical significance was set at an alpha level of 5%.

RESULTS

The prevalence of DR among the CVA patients was 79%. The haemorrhagic type of CVA was the predominant type, accounting for 59% of cases, while ischaemic stroke accounted for 41%.

The majority had moderate NPDR, comprising 44% of the cases [Table/Fig-1]. Additionally, 35% of patients had Random Blood Sugar Levels (BSL-R) between 201-300 mg/dL and 63% of patients had HbA1c levels below 7.6%.

In the present study, patients with DR had a mean±SD age of 57.13±7.63 years, while those without DR had a mean age of 51.48 years. The mean BSL-R was 218.2 mg/dL in patients with DR and 177.33 mg/dL in those without. Furthermore, the mean HbA1c level was 7.29% among patients with DR and 5.87% among those without [Table/Fig-2]. Patients with DR were notably older and had higher BSL-R and HbA1c values compared to those without DR (p-values: 0.005, <0.001 and <0.001, respectively) [Table/Fig-3]. A significant association was found between older age and the presence of DR (p-value: 0.015). However, no significant association was observed between gender and DR (p-value=0.887) [Table/Fig-4].

Among the 100 CVA patients, 59 had haemorrhagic stroke and 41 had ischaemic stroke. Of the 59 patients with haemorrhagic stroke, 46 (58.6%) had DR, while among the 41 patients with ischaemic stroke, 33 (41.8%) had DR. No association was found between DR and the type of stroke (p-value: 0.761) [Table/Fig-5].

Parameters	Sub groups	Frequency (n)
DR severity	No DR	21
	Mild DR	20
	Moderate DR	44
	Severe DR	15
BSL-R	<140 mg/dL	2
	140-200 mg/dL	61
	201-300 mg/dL	35
	>300 mg/dL	2
HbA1C	<7.6 gm%	63
	7.6-9.5 gm%	36
	>9.5 gm%	1

[Table/Fig-1]: Severity of Diabetic Retinopathy (DR) and glycaemic profile of study participants.

Diabetic Retinopathy (DR)	Yes				No			
	Mean	Median	Std. deviation	IQR	Mean	Median	Std. deviation	IQR
Age (years)	57.13	56.00	7.63	50,65	51.48	51.00	6.36	47,56.5
HbA1C	7.29	7.40	1.05	6.2,8	5.87	6.00	0.53	5.7,6
BSL-R	218.25	200.00	45.54	190,250	177.33	170.00	35.06	150,200

[Table/Fig-2]: Clinical profile of patients with and without Diabetic Retinopathy (DR).

Parameters	Diabetic Retinopathy (DR)	n	Mean rank	Sum of ranks	p-value
Age	Yes	79	54.74	4324.50	0.005*
	No	21	34.55	725.50	
	Total	100			
HbA1C	Yes	79	58.03	4584.00	<0.001*
	No	21	22.19	466.00	
	Total	100			
BSL-R	Yes	79	56.13	4434.50	<0.001*
	No	21	29.31	615.50	
	Total	100			

[Table/Fig-3]: Association between demographic and clinical profile of patients with and without Diabetic Retinopathy (DR).
*The p-value <0.05 was considered statistically significant

Variables		Diabetic Retinopathy (DR)		p-value
		Yes, n (%)	No, n (%)	
Age	40-49 years	17 (21.5))	9 (42.9)	0.015*
	50-59 years	30 (38)	10 (47.6)	
	60-69 years	32 (40.5)	2 (9.5)	
Gender	Male	40 (50.6)	11 (52.4)	0.887
	Female	39 (49.4)	10 (47.6)	
Total		79 (100)	21 (100)	

[Table/Fig-4]: Association between age, gender and Diabetic Retinopathy (DR).

Diagnosis	Diabetic Retinopathy (DR)		p-value
	Yes, n (%)	No, n (%)	
Haemorrhagic stroke, n (%)	46 (58.2%)	13 (61.9%)	0.761
Ischaemic stroke, n (%)	33 (41.8%)	8 (38.1%)	
Total, n (%)	79 (100)	21 (100)	

[Table/Fig-5]: Association between type of CVA and Diabetic Retinopathy (DR).

Among the patients, 63 had HbA1c levels below 7.6%, with 42 of them also having DR. As HbA1c levels increased, the prevalence of DR also increased. Specifically, 36 patients had HbA1c levels between 7.6% and 9.5% and one patient had an HbA1c level exceeding 9.5%, all of whom had DR. There was a significant

association between higher HbA1c levels and DR (p-value <0.001) [Table/Fig-6].

HbA1C (%)	Diabetic Retinopathy (DR)		p-value
	Yes, n (%)	No, n (%)	
<7.6	42 (53.2)	21 (100)	<0.001*
7.6-9.5	36 (45.6)	0	
>9.5	1 (1.3)	0	
Total	79 (100)	21 (100)	

[Table/Fig-6]: Association between HbA1C and Diabetic Retinopathy (DR).

A significant association between BSL-R and HbA1c with the severity of DR was found (p-value <0.001). Higher BSL-R and HbA1c values were associated with increased severity of DR (p-value <0.001) [Table/Fig-7].

Parameters	DR severity	n	Mean rank	p-value
BSL-R	No DR	21	29.31	<0.001*
	Mild NPDR	20	34.17	
	Moderate NPDR	44	59.22	
	Severe NPDR	15	76.37	
	Total	100		
HbA1C	No DR	21	22.19	<0.001*
	Mild NPDR	20	26.95	
	Moderate NPDR	44	62.58	
	Severe NPDR	15	86.10	
	Total	100		

[Table/Fig-7]: Association between BSL-R and HbA1C with severity of Diabetic Retinopathy (DR).

DISCUSSION

The DR is a common microvascular complication affecting approximately one-third of individuals with DM, making it a leading cause of vision loss among working-age adults. This condition reflects a systemic microcirculatory disorder that impacts not only the eyes but also other vital organs, such as the brain [10]. This shared microvascular pathology between the brain and eyes provides a compelling basis for exploring the underlying mechanisms linking CVAs and DR.

Previous studies have primarily focused on investigating the incidence of CVAs, their risks among patients with DR and subsequent outcomes [11-13]. For instance, a systematic review and meta-analysis of 19 cohort studies encompassing 81,452 patients with DM analysed the association between DR and increased CVA risk. The present study identified DR as a significant indicator for predicting strokes [11]. Another study conducted a record-based secondary data analysis involving 2,828 patients confirmed an association between DR and elevated stroke risk during the follow-up period. This underscores DR as an indicator linked to a heightened likelihood of stroke, suggesting that the microvascular changes characteristic of DR may have broader implications for cerebrovascular health [12].

In a prospective study by Venkatesh P et al., in New Delhi, India, involving 170 patients, researchers assessed various morbidities, including strokes, across different DR grades. They observed a significant correlation between nephropathy, neuropathy and macrovascular co-morbidities among patients in the early stages of DR [13]; however, in the present study, no significant association was found between DR and the type of stroke.

In the present study, the majority of participants exhibited moderate NPDR at 44%, followed by mild NPDR at 20% and severe NPDR at 15%. This distribution aligns with findings from Cheung N et al., who similarly observed that most cases of DR fell within the mild to moderate categories [14].

Wong KH et al., reported that patients with mild to severe DR faced an elevated risk of stroke [12]. In the current study, the majority of patients were over 50 years old, with the mean age of stroke patients being 51.48 years in those without DR (non DR patients) and 57.13 years in those with DR (DR patients). This finding suggests that patients with DR and stroke tended to be older (p-value=0.005). Previous literature has consistently identified older age as a significant risk factor for DR [15].

No significant association was found between gender and DR in the current study (p-value=0.887). However, Wong KH et al., reported a higher proportion of males with stroke in their study (75.2%). It is well-documented that stroke can exhibit differences between males and females in terms of risk factors, clinical presentation, treatment response and complications [12].

Haemorrhagic stroke was the predominant type in the present study, occurring in 59% of cases, followed by ischaemic stroke at 41%. There was no significant association between the type of CVA and the presence of DR (p-value=0.761). In contrast, Shah K et al., in their prospective study involving 2,500 patients with diabetes, reported that 83.82% of stroke-related deaths among individuals with DR were ischaemic in nature [16].

In the present study, the mean random blood glucose levels were notably higher among patients with DR (218.2 mg/dL) compared to those without (177.33 mg/dL), indicating poorer diabetic control among the former group. A significant association was also observed between the severity of DR and higher random blood glucose levels (p-value<0.001). Similarly, Cheung N et al., reported elevated fasting sugar levels in DR patients (mean range: 212.8 to 218.2 mg/dL), whereas those without DR had a lower mean fasting sugar level of 156.8 mg/dL [14].

Furthermore, HbA1c levels were significantly higher among stroke patients with DR (mean: 7.29%) compared to those without (mean: 5.87%), indicating long-term poor glycaemic control in the former group (p-value<0.001). Wong KH et al., reported even higher mean HbA1c levels among stroke patients (mean: 8.5%) compared to this study [12].

Limitation(s)

The applicability of the findings may be limited since the study focused solely on patients from one hospital. As the present study employed a descriptive and cross-sectional design, the authors were unable to determine causal relationships between DR and the variables examined. Furthermore, the lack of a comparison group (patients without CVAs) restricts our ability to draw definitive conclusions about the relationship between DR and CVA. Additionally, the study's small sample size may impact the robustness of the results.

CONCLUSION(S)

In the present study, 79% of patients with DM who had experienced a CVA also had DR, with moderate NPDR being the most prevalent type in this cohort. Patients with DR were significantly older and exhibited higher BSL-R and HbA1c levels compared to those without retinopathy. Furthermore, the severity of DR was strongly linked to increased BSL and HbA1c values. Among patients with DR, haemorrhagic stroke was the most commonly observed type of CVA. However, no significant association was found between the type of CVA and the severity of DR. To enhance the validity and generalisability of these findings, further multicentric, analytical and prospective studies are warranted.

REFERENCES

[1] Deshmukh CD, Jain A. Diabetes mellitus: A review. Int. J. Pure App. Biosci. 2015;3(3):224-30.
[2] Yau JWY, Rogers SL, Kawasaki R, Lamoureux EL, Kowalski JW, Bek T, et al. Global prevalence and major risk factors of diabetic retinopathy. Diabetes Care. 2012;35:556-64. Doi: 10.2337/dc11-1909.

[3] Cheung N, Mitchell P, Wong TY. Diabetic retinopathy. Lancet. 2010;376:124-36. Doi: 10.1016/S0140-6736(09)62124-3.
[4] Park S, Rhee SY, Jeong SJ, Kim K, Chon S, Yu SY, et al. Features of long-standing Korean type 2 diabetes mellitus patients with diabetic retinopathy: A study based on standardized clinical data. Diabetes Metab J. 2017;41:393-404. Doi:10.4093/dmj.2017.41.5.393.
[5] Global, regional, and national burden of stroke, 1990-2016: A systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2019;18:439-58. Doi:10.1016/S1474-4422(19)30034-1.
[6] Abramson JH. WINPEPI (PEPI-for-Windows): Computer programs for epidemiologists. Epidemiol Perspect Innov. 2004;1(1):6. Doi: 10.1186/1742-5573-1-6.
[7] Sapra A, Bhandari P. Diabetes. [Updated 2023 Jun 21]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK551501.
[8] Khaku AS, Tadi P. Cerebrovascular Disease. [Updated 2023 Aug 7]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK430927/.
[9] Salmon FJ. Kanski's Clinical Ophthalmology. 9th ed. Amsterdam: Elsevier; 2019.
[10] van Sloten TT, Sedaghat S, Carnethon MR, Launer LJ, Stehouwer CDA. Cerebral microvascular complications of type 2 diabetes: Stroke, cognitive dysfunction, and depression. Lancet Diabetes Endocrinol. 2020;8:325-36. Doi: 10.1016/S2213-8587(19)30405-X.
[11] Hu K, Jiang M, Zhou Q, Zeng W, Lan X, Gao Q, et al. Association of diabetic retinopathy with stroke: A systematic review and meta-analysis. Front Neurol. 2021;12:626996. Doi: 10.3389/fneur.2021.626996.
[12] Wong KH, Hu K, Peterson C, Sheibani N, Tsivgoulis G, Majersik JJ, et al. Diabetic retinopathy and risk of stroke. Stroke. 2020;51(12):3733-36. Doi: 10.1161/STROKEAHA.120.030350.
[13] Venkatesh P, Tibrewal S, Bhowmik D, Tripathi M, Ramakrishnan S, Vashist N, et al. Prevalence of systemic co-morbidities in patients with various grades of diabetic retinopathy. Indian J Med Res [Internet]. 2014;140(1). Available from: https://journals.lww.com/ijmr/fulltext/2014/40010/prevalence_of_systemic_co_morbidities_in_patients.13.aspx.
[14] Cheung N, Rogers S, Couper DJ, Klein R, Sharrett AR, Wong TY. Is diabetic retinopathy an independent risk factor for ischemic stroke? Stroke. 2007;38(2):398-401. Doi: 10.1161/01.STR.0000254547.91276.50. Available from: https://doi.org/10.1161/01.STR.0000254547.91276.50.
[15] Namperumalsamy P, Kim R, Vignesh TP, Nithya N, Royes J, Gijo T, et al. Prevalence and risk factors for diabetic retinopathy: A population-based assessment from Theni District, south India. Br J Ophthalmol. 2009;93(4):429-34.
[16] Shah K, Sundaram N, Raut SR, Rao K, Wadhwa N. Diabetic retinopathy grade as a predictive marker of stroke and mortality in Type 2 diabetes mellitus patients with amputations-seven-year follow-up. Diabetes. 2018;67(Suppl 1):603-P. Available from: https://doi.org/10.2337/db18-603-P.

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